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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,356	02/17/2004	Jian-Qiang Fan	04168/100M413-US1	9219

7278 7590 01/12/2006

DARBY & DARBY P.C.
P. O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,356	FAN, JIAN-QIANG	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *6,10-13,21,25-28,33 and 38-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-9,14-20,22-24,29-32 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/19/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 10/20/05.

Claims 1-40 are pending.

Claims 6, 11-13, 21, 26-28, 33, and 38-40 were withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species. During a telephone conversation with Stephanie Amoroso on 5/31/05 a provisional election was made with traverse to prosecute the invention of 1-deoxygalactonojirimycin, readable on claims 1-5, 7-10, 14-20, 22-25, 29-32, and 34-37. Ms. Amoroso informed the Examiner that 1-deoxygalactonojirimycin was not an active site-specific chaperone for beta-glucocerebrosidase, and so did not read on claims limited to active site specific chaperones from this protein (i.e. claims 6, 21, and 33). Applicant did not set forth any grounds for traversal in the response filed 11/20/05, so the restriction requirement is made FINAL.

In the listing of the claims filed 10/20/05, Applicant indicated that claim 25 was withdrawn. Claim 25 had been considered in the last action because the Examiner thought that the first of the three depicted structures embraced the elected species, 1-deoxygalactonojirimycin. However, this was incorrect. In order for this structure to embrace 1-deoxygalactonojirimycin the R_2 group attached to the N atom would have to be an H, while the R_2 group attached to the C atom at position 2 would simultaneously have to be a hydroxyl. The claim does not allow for this because, while it states that "R_2 and $R_{2'}$ independently represent H, OH, or a C_1-C_{12} alkyl group", it does not indicate that each instance of R_2 is independently H, OH, or a C_1-C_{12} alkyl group, instead it

allows for only one identity for R_2 per structure. So claim 25 does not embrace the elected species and is properly withdrawn, as are the previous rejections of it. For the same reasons claim 10 does not embrace the elected species and it is also withdrawn, as are the previous rejections of it. Note the at claim 10 depends from withdrawn claim 6.

Claims 1-5, 7-9, 14-20, 22-24, 29-32, and 34-37 and the species of 1-deoxygalactonojirimycin are under consideration in this Office Action.

Drawings

The Application as filed contained no drawings.

Claim Objections

Applicant's amendment to claim 6 was sufficient to overcome the objection.

Rejections Withdrawn

The rejection of claims 4, 29-32 and 34-37 for indefiniteness is withdrawn in view of Applicant's amendment.

The rejection of claims 29-32, and 34-37 for lack of adequate written description is withdrawn in view of Applicant's amendment.

The rejection of claims 1-5, 7-9, 14-20, 22-24, 29-32, and 34-37 for lack of adequate enablement is withdrawn in view of Applicant's amendment.

The double patenting rejections of claims 1-5, 7-9, 14-20, 22-24, 29-32, and 34-37 are withdrawn in view of the terminal disclaimer filed over US Patents 6,274,597, 6,589,964, 6,599,919, and 6,774,135.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7-9, 14-17, 19, 20, 22-24, 29-32, and 34-37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Yew et al (US Patent 6,066,626) taken with Fan et al (US Patent 6,274,597).

Yew taught methods of providing biologically active human alpha galactosidase-A to cells of an individual having a deficiency of that enzyme (Fabry's disease) by administration into cells of the individual an adenoviral expression construct encoding alpha galactosidase. See claim 8. The cells may be in vivo (see claims) or ex vivo (see column 9, lines 10-14).

Yew did not teach an active site-specific chaperone.

Fan '597 taught methods of increasing the activity of a mutant form of lysosomal alpha galactosidase-A in mammalian cells, and treating Fabry's disease in an individual, comprising administering an effective amount of 1-deoxygalactonojirimycin. See claims 1-7.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat an individual with Fabry's disease by administering both the expression construct of Yew, and 1-deoxygalactonojirimycin. One would have been motivated to augment the method of Yew by combining it with the method of Fan above because, in addition to providing the wild type protein of Yew, one would have expected to obtain activity from the patient's endogenous mutant protein as a result of the method of Fan, thereby providing more alpha galactosidase-A activity than would have been obtainable by the separate methods.

Thus the invention as a whole was prima facie obvious.

Claims 1-5, 7-9, 14-17, 19, 20, 22-24, 29-32, and 34-37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Yew et al (US Patent 6,066,626) taken with and any one of Fan et al (US Patent 6,589,964, issued 7/8/2003), Fan et al (US Patent 6,599,919 issued 7/29/2003), or Fan et al (US Patent 6,774,135, issued 8/10/2004).

The applied references Fan et al (US Patent 6,589,964, issued 7/8/2003), Fan et al (US Patent 6,599,919 issued 7/29/2003), and Fan et al (US Patent 6,774,135, issued 8/10/2004) have a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, they constitute prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Yew taught methods of providing biologically active human alpha galactosidase-A to cells of an individual having a deficiency of that enzyme (Fabry's disease) by administration into cells of the individual an adenoviral expression construct encoding alpha galactosidase. See claim 8. The cells may be in vivo (see claims) or ex vivo (see column 9, lines 10-14).

Yew did not teach an active site-specific chaperone.

Fan '964 taught methods of enhancing in a mammalian cell the activity of an enzyme, which method comprises administering a competitive inhibitor of the enzyme in an amount effective to enhance enzyme activity. See claim 1. Fan also taught methods of increasing the activity of a mutant form of lysosomal alpha galactosidase-A in mammalian cells, and treating Fabry's disease in an individual, comprising administering an effective amount of 1-deoxygalactonojirimycin. See e.g. claims 1-10, and 41-47, especially claims 9, 10 and 47.

Fan '919 taught methods of enhancing in a mammalian cell the activity of an enzyme, which enzyme when mutated tends to fold in an incorrect conformation in endoplasmic reticulum (ER), and whereby a level of the active enzyme is deficient as a result of such mutation, which method comprises administering a competitive inhibitor of the enzyme in an amount effective to enhance enzyme activity. Fan also taught such a method wherein the competitive inhibitor is 1-deoxygalactonojirimycin. Fan also taught methods of treating a glycosphingolipid storage disease by administering 1-deoxygalactonojirimycin. See claims 1-16, and 18-42, especially claims 18 and 19.

Fan '135 taught methods of treating Fabry's disease comprising administering to an individual in need thereof an effective amount of 1-deoxygalactonojirimycin. See claims 1, 3, 4, 7, 9, 10, 12, 13, 15-17, 21, 23-25, 29, and 31-36.

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat an individual with Fabry's disease by administering both the expression construct of Yew, and 1-deoxygalactonojirimycin. One would have been motivated to augment the method of Yew by combining with any of the methods of Fan above because, in addition to providing the wild type protein of Yew, one would have expected to obtain activity from the patient's endogenous mutant protein as a result of the methods of Fan, thereby providing more alpha galactosidase-A activity than would have been obtainable by the separate methods.

Thus the invention as a whole was prima facie obvious.

Claims 17 and 18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Yew et al (US Patent 6,066,626) taken with Fan et al (US Patent 6,274,597) as applied to claims 1-5, 7-9, 14-17, 19, 20, 22-24, 29-32, and 34-37 above, and further in view of Hendricks et al (Blood 96 (11 part 1): 845a, 2000).

The teachings of Yew and Fan are discussed above, and can be combined to render obvious methods of increasing the level of expression of alpha galactosidase in an individual by administering to the individual cells comprising an alpha galactosidase expression vector and 1-deoxygalactonojirimycin.

Yew and Fan did not teach administration of human primary cells or mesenchymal stem cells comprising an alpha galactosidase expression vector.

Hendricks taught a method in which human mesenchymal stem cells were transduced with a retroviral expression vector encoding alpha galactosidase A, and then were implanted into mice where they secreted high levels of alpha galactosidase A suggesting their usefulness as gene delivery vehicles for the treatment of Fabry's disease. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer human mesenchymal stem cells comprising an alpha galactosidase A expression vector to a human individual for the purpose of increasing the expression level of alpha galactosidase A in the individual. One would have been motivated to do so because Hendricks suggests that human mesenchymal stem cells transduced to express alpha galactosidase A would be useful as gene delivery vehicles for the treatment of Fabry's disease.

Thus the invention as a whole was prima facie obvious.

Claims 17 and 18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Yew et al (US Patent 6,066,626) taken with any one of Fan et al (US Patent 6,589,964, issued 7/8/2003), Fan et al (US Patent 6,599,919 issued 7/29/2003), or Fan et al (US Patent 6,774,135, issued 8/10/2004) as applied to claims 1-5, 7-10, 14-17, 19, 20, 22-24, 29-32, and 34-37 above, and further in view of Hendricks et al (Blood 96 (11 part 1): 845a, 2000).

The teachings of Yew and Fan '964, '919, and '135 are discussed above and can be combined to render obvious methods of increasing the level of expression of alpha galactosidase in an individual by administering to the individual cells comprising an alpha galactosidase expression vector and 1-deoxygalactonojirimycin.

Yew and Fan did not teach administration of human primary cells or mesenchymal stem cells comprising an alpha galactosidase expression vector.

Hendricks taught a method in which human mesenchymal stem cells were transduced with a retroviral expression vector encoding alpha galactosidase A, and then were implanted into mice where they secreted high levels of alpha galactosidase A suggesting their usefulness as gene delivery vehicles for the treatment of Fabry's disease.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer human mesenchymal stem cells comprising an alpha galactosidase A expression vector to a human individual for the purpose of increasing the expression level of alpha galactosidase A in the individual. One would have been motivated to do so because Hendricks suggests that human mesenchymal stem cells transduced to express alpha galactosidase A would be useful as gene delivery vehicles for the treatment of Fabry's disease.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 10/20/05 have been fully considered but they are not persuasive.

Applicant argues at page 16 of the response that MPEP 706.02(l)(1)-(3) states that subject matter that is prior art only under 35 USC 102(e) is disqualified as prior art under 35 USC 103(c) if that subject matter and the claimed invention were owned by the same person or subject to an obligation of assignment to the same person at the time the invention was made. Applicant asserts that Exhibit 1 Tabs A-D are copies of the assignments of the '597, '919, and '964 patents, acknowledging that the assignee is Mount Sinai School of Medicine of New York University.

This is unpersuasive for several reasons. First, the Office did not receive exhibit 1. Second, even if exhibit one had been received, there is no clear statement in the response that the inventions were commonly owned at the time the invention was made. The fact that the reference and the application have the same assignee is not, by itself, sufficient evidence to disqualify the prior art under 35 U.S.C. 103(c). There must be a statement that the common ownership was "at the time the invention was made." See MPEP 706.02(l)(1). Third, the '597 patent was issued on 8/14/01, more than one year prior to the earliest claimed priority date of the instant application (2/8/03), so it is not equivalent to a reference available under only 35 USC 102(e). For this reason, the obviousness rejections over the '597 patent cannot be overcome by establishing common ownership with the instant application at the time of invention. Fourth, the response does not address the rejections over the '135 patent.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635